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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,426	03/25/2005	Ferdinand Hermann Bahlmann	P/2107-264	5804

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OSTROLENK FABER GERB & SOFFEN
1180 AVENUE OF THE AMERICAS
NEW YORK, NY 100368403

EXAMINER	
HEARD, THOMAS SWEENEY	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
04/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,426	BAHLMANN ET AL.	
	Examiner	Art Unit	
	THOMAS S. HEARD	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-107* is/are pending in the application.

4a) Of the above claim(s) *44,45,47-51,54-58,60-64,66-69,71-89 and 91-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46, 52, 53, 59, 65, 70, and 90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Applicants Amendments to the claims received on 12/29/2008 is acknowledged. The text of those sections of Title 35 U.S. Code not included in the action can be found in the prior office action. Rejections or objections not addressed in this office action with respect to the previous office action mailed 6/23/2008 are hereby withdrawn.

Claim(s) 44-107 are pending. Claims 44, 45, 47-51, 54-58, 60-64, 66-69, 71-89, and 91-107 are withdrawn. Claims 46, 52, 53, 59, 65, 70, and 90 are hereby examined on the merits.

Claim Rejections - 35 USC § 103

Applicant's arguments with respect to Claims 46, 52, 53, 59, 65, 70, and 90 have been considered but are moot in view of the new ground(s) of rejection set forth below. The 103(a) rejection set forth in the Office Action mailed 6/23/2008 is hereby withdrawn in light of a new search and consideration.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 46, 52, 53, and 90 rejected under 35 U.S.C. 102(e) as being anticipated by Smith-Swintosky et al US 2003/0130197.

The instant invention is drawn to a method of treatment for wound healing through the weekly dosis of 1 to 90 international units (IU) EPO/kg body weight to a subject in need of said treatment. The routes of administration are those of parenteral (intravenous), and the EPO (erythropoietin) is animal or human.

Smith-Swintosky et al US 2003/0130197, discloses the administration of EPO over three days, i.v., at 1.32 I.U. per day where the rats were rendered ischemic through a surgical procedure to test for EPO's ability to treat the resulting would, anticipating the method of Claims 46, 52, and 53, see Example 5 and the study design in column 2 of page 12 of the specification. The EPO administered was animal anticipating readable on Claim 90. The three day experiment of the i.v. infusion administered 1.32 I.U./day for three days with the rats weighs at .200 to 0.250 kg, results in a dosage in the lower range of 1 to 90 IU EPO/kg and within the time period of one week (weekly dosage).

Applicants define wound as

[0045] A "wound" means in connection with the present invention an interruption of the coherence of body tissues with or without loss of substance and caused by mechanical injury or physically caused cell damage. Types of wound are mechanical wounds, thermal wounds, chemical wounds, radiation wounds and disease-related wounds. Mechanical wounds arise through traumatic violence and occur in particular as incision and puncture wounds, crushing, lacerating, tearing and abrading wounds, scratch and bite wounds and projective wounds. Thermal wounds arise through exposure to heat or cold. Chemical wounds arise in particular through the action of acids or alkalis. Radiation wounds arise for example through exposure to actinic and ionizing radiation. Wounds occurring in relation to disease are in particular congestion-related wounds, traumatic wounds, diabetic wounds etc. The invention provides in

particular for erythropoietin to be administered preferably topically or intravenously for wound healing.

Because the injury was performed on the rat as described in Example 5, and was done to the central nervous system, ischemia is readable on the term wound.

Therefore, the invention as claimed is anticipate by the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

For the purpose of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. V. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held in accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976);In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

Claims 46, 52, 53, 59, 65, 70, and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Smith-Swintosky et al US 2003/0130197; in view of

Krussel JS, et al, "Vascular endothelial growth factor (VEGF) mRNA splice variants are differentially expressed in human blastocysts," Mol Hum Reprod. 2001 Jan;7(1):57-63;

Janquet, Kai, et al., "BRIEF COMMUNICATION, Erythropoietin and VEGF Exhibit Equal giogenic Potential, June 25, 2002, Pages 326-333 (from Applicant's IDS);

Amgen Inc, EP 0613683 A1;

Zaharia Czeizler, US 6,274,158; and

Westenfelder, US 6,748,154, for definition of subpolycythemic erythpoietin dosis and ranges, the two US Patents, EP 0613683, and Krussel JS, et al were made of record in the previous office action.

The instantly claimed invention is drawn to a method for wound healing through the administration of a subpolycythemic erythropoietin (EPO) dosis and an ingredient that stimulates endothelial progenitor cells.

Smith-Swintosky et al US 2003/0130197, discloses the administration of EPO over three days, i.v., at 1.32 I.U. per day where the rats were rendered ischemic, anticipating the method of Claims 46, 52, and 53, see Example 5 and the study design in column 2 of page 12 of the specification. The EPO administered was animal anticipating readable on Claim 90. The three day experiment of the i.v. infusion administered 1.32 I.U./day for three days with the rats weighs at .200 to 0.250 kg,

results in a dosage in the range of 1 to 90 IUEPO/kg within the time period of one week (weekly dosage). Smith-Swintosky et al does not teach oral or pulmonary administration of EPO nor does Smith-Swintosky et al teach an additional ingredient which stimulates endothelial progenitor cells.

Westenfelder, US 6,748,154, the definition of subpolycythemic erythpoietin dosis and ranges as being about 250-350 U/kg body weight, indicating that ranges less than this do not induce polycythemia, see column 6 and line 45 onward for example. Thus, any EPO dosage within this range or lower would be a subpolycythemic erythpoietin dosis because it would not induce polycythemia.

Zaharia Czeizler, US 6,274,158 further teaches the oral, subcutaneous, and intravenous administration of EPO for the treatment of bleeding due to surgical treatments (wounds made by the surgical process), for example, see abstract and claim 32 for example. Amgen Inc, EP 0613683 A1, teaches EPO may be formulated for inhalers (Pulmonary administration), see abstract. Zaharia Czeizler and Amgen's references are readable upon Claims 59, 65, and 90.

Krussel JS, et al teaches the compound VEGF (vascular endothelial growth factor) stimulates endothelial progenitor cells and induces angiogenesis; see Introduction and column 2, readable on Claim 70. Applicants have define wound healing as: "*In connection with the present invention, 'wound healing' means the physiological processes for regenerating damaged tissue* [treatment of wounds] *and for closing a wound, especially formation of new connective tissue and capillaries.*" Therefore, VEGF is viewed as a compound that not only is a compound that induces

angiogenesis (capillary formation) but is also a compound that heals wound by Applicant's definition.

Jaquet, Kai, et al teaches the EPO and VEGF exhibit equal and angiogenic potential and that VEGF has been shown to enhance angiogenesis in ischemic diseases, see Introduction of the article.

It would have been obvious at the time of instantly claimed invention to use EPO for the purposes and benefits of wound healing in ischemic tissue as taught by Smith-Swintosky et al. It would also have been obvious to use EPO in combination with VEGF for wound healing as it is obvious to combine two compositions to form a third composition that performs the same function, readable on Claims 70. One would have been motivated to do so given Smith-Swintosky et al clear teaching of wound healing properties of EPO (treatment of ischemia) and Krussel's teaching that VEGF induces angiogenesis, an important part of wound healing from Applicant's definition of wound healing. Although Zaharia Czeizler, US 6,274,158, does not teach the instant method of using a composition comprising the specifically claimed concentrations of EPO at the particular dosage of 1 to 90 IU EPO/kg, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have optimized the concentration for administration of EPO for different wounds and different formulations and routes of administration taught by the references supra. In other words, given the general teaching that subpolycythemic erythpoietin dosis are beneficial for the treatment of ischemia, as taught by Smith-Swintosky et al, one of ordinary skill in the art would be

motivated to optimize the whole of the invention in the amounts of EPO and VEGF in the treatment of ischemia (wound).

Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Response to Applicants Arguments

Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection, especially in light of the new rejection set forth supra. Applicant's arguments are addressed here to the extent they read on the new rejection, and these arguments are moot because the prior art teaches the subpolycythemic erythpoietin dosis ranges as evidenced by the new references.

Response to Amendment

The affidavit under 37 CFR 1.132 filed 12/29/2008 is insufficient to overcome the rejection of Claim 46, 52, 53, 59, 65, 70, and 90 based upon 103(a) as set forth in the last Office action.

In the evidence set forth to show unexpected result is unclear and incomplete. Proper controls for demonstrating an unexpected result are not evident. First, the labeling of the graphs is not clear as there are three white bars and one black bar, and no clear indication of which way one should read the graph, see Exhibit 8, Day 3, for example. A diabetic model is presented, and it appears that only a low dose was tested for the diabetic model. There are two placebos, non-diabetic and diabetic. There were two tests, diabetic low-dose EPO and non-diabetic high-dose EPO. There is no diabetic high-dose EPO or non-diabetic low-dose EPO. Thus, the experiment is incomplete and lacks evidence of unexpected results.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Prior art contained in the reference of record can be applied in the next office action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas S. Heard whose telephone number is (571) 272-2064. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thomas S Heard/
Examiner, Art Unit 1654

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654